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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER
YOUNG, JOSEPHINE

ART UNIT	PAPER NUMBER
1623	

DATE MAILED: 07/07/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/587,662	Applicant(s) AU ET AL.	
	Examin r Josephine Young	Art Unit 1623	

-- The MAILING DATE of this communication appears on the cover sh et with th correspondenc address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 May 2003 and 30 April 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-92* is/are pending in the application.

4a) Of the above claim(s) *25,29-32,36-39 and 48-89* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-24,26-28,33-35,40-47 and 90-92* is/are rejected.

7)☒ Claim(s) *91 and 92* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *5* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restriction Set Forth in the Office Action Mailed

September 9, 2002 and December 30, 2002

Applicant's election with traverse of Group I in Paper No. 8, filed October 9, 2002, is acknowledged. Because Applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). The requirement is still deemed proper and is therefore made FINAL.

Claims 29-32, 36-39, 49-89 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim.

Applicant's election with traverse of the species directed to methods for inhibiting or reducing the growth of a cell or for treating cancer comprising administering paclitaxel (A1) and a nucleoside or nucleotide analog such as AZT and d4T (B1), recited in claims 1-24, 26-28, 33-35 and 40-47, in paper nos. 14 and 15, filed April 30, 2003 and May 16, 2003, respectively, is acknowledged. Because Applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). The requirement is still deemed proper and is therefore made FINAL.

Claims 25 and 48 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim.

Further, the examination of the generic claims is limited to the embodiments directed to the use of paclitaxel (A1) and a nucleoside or nucleotide analog such as AZT and d4T (B1).

Rejections Set Forth in the Office Action dated December 30, 2002

Claims 1-24, 26-28, 33-35 and 40-47 were rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating cancer related to certain cell lines, does not reasonably provide enablement for treating all types of cancer.

Claims 1-24, 28, 33-35 and 40-45 were rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating cancer using a specific telomere damage-inducing agent, namely paclitaxel, and telomerase inhibitory agent, namely AZT or d4T, does not reasonably provide enablement for treating cancer using paclitaxel and any nucleoside or nucleotide analog other than AZT or d4T.

Claims 41 and 43 were rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for identifying patients having cancer, does not reasonably provide enablement for identifying patients about to have cancer.

Claims 1-24, 26-28, 33-35 and 40-47 were rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention by using the term "telomere damage inducing agent".

Claims 1-4, 8-10, 12-14, 16, 18, 20, 22-24, 26, 33-35 and 40-46 were rejected under 35 U.S.C. 102(b) as anticipated by the patent US 5,756,537 to GILL.

Claims 1-24, 26-28, 33-35 and 40-47 were rejected under 35 U.S.C. 103(a) as being unpatentable over the patent US 6,150,398 to VANDE WOULDE et al. in view of THE MERCK INDEX, **1996**, 7117, 8958 and 10252.

Claims 1-24, 26, 28, 33-35 and 40-46 were rejected under 35 U.S.C. 103(a) as being unpatentable over the article MELANA et al., Clinical Cancer Research, March **1998**, *4*, 693-696 in view of THE MERCK INDEX.

Claims 1-24, 26-28, 33-35 and 40-47 were rejected under 35 U.S.C. 103(a) as being unpatentable over the article MELANA in view of THE MERCK INDEX and further in view of the article PAI et al, Cancer Research, May **1998**, *58*, 1909-1913.

Claims 1-4, 7-24, 26-28, 33-35 and 40-47 were rejected under 35 U.S.C. 103(a) as being unpatentable over GILL in view of THE MERCK INDEX.

Response to Amendments filed April 30, 2003 and May 16, 2003

In the amendments filed April 30, 2003 and May 16, 2003, claims 1, 2, 24, 26, 27, 33, 34, 40-43 and 45-47 were amended. Claims 90-92 were added.

An action on the merits of claims 1-24, 26-28, 33-35, 40-47 and 90-92 is contained herein below.

In regards to the Rejection of claims 1-24, 26-28, 33-35 and 40-47 under 35 U.S.C. 112, first paragraph, because the specification does not reasonably provide enablement for treating all types of cancer, Applicant's amendments filed April 30, 2003 and May 16, 2003 have been fully considered and have overcome the Rejection set forth in the Office Action dated December 30, 2002 (see paper no. 13, Inventor's Declaration under 37 C.F.R. 1.132, filed April 30, 2003).

In regards to the Rejection of claims 1-24, 28, 33-35 and 40-45 under 35 U.S.C. 112, first paragraph, because the specification does not reasonably provide enablement for treating cancer using paclitaxel and any nucleoside or nucleotide analog other than AZT or d4T, Applicant's amendments filed April 30, 2003 and May 16, 2003 have been fully considered but they are not persuasive. The Rejection of the claims is maintained for the reasons of record as set forth in the Office Action dated December 30, 2002.

In regards to the Rejection of claims 41 and 43 under 35 U.S.C. 112, first paragraph, because the specification does not reasonably provide enablement for identifying patients about to have cancer, Applicant's amendments filed April 30, 2003 and May 16, 2003 have been fully considered and have overcome the Rejection set forth in the Office Action dated December 30, 2002 (claims amended).

In regards to the Rejection of claims 1-24, 26-28, 33-35 and 40-47 under 35 U.S.C. 112, second paragraph, for containing the term "telomere damage inducing agent," Applicant's amendments filed April 30, 2003 and May 16, 2003 have been fully considered and have overcome the Rejection set forth in the Office Action dated December 30, 2002 (claims amended).

In regards to the Rejection of claims 1-4, 8-10, 12-14, 16, 18, 20, 22-24, 26, 33-35 and 40-46 under 35 U.S.C. 102(b) as anticipated by GILL, Applicant's amendments filed April 30, 2003 and May 16, 2003 have been fully considered but they are not persuasive. The Rejection of the claims is maintained for the reasons of record as set forth in the Office Action dated December 30, 2002.

In regards to the Rejection of claims 1-24, 26-28, 33-35 and 40-47 under 35 U.S.C. 103(a) as being unpatentable over VANDE WOULDE in view of THE MERCK INDEX, Applicant's amendments filed April 30, 2003 and May 16, 2003 have been fully considered and have overcome the Rejection set forth in the Office Action dated December 30, 2002.

In regards to the Rejection of claims 1-24, 26, 28, 33-35 and 40-46 under 35 U.S.C. 103(a) as being unpatentable over MELANA in view of THE MERCK INDEX, Applicant's amendments filed April 30, 2003 and May 16, 2003 have been fully considered and have overcome the Rejection set forth in the Office Action dated December 30, 2002.

In regards to the Rejection of claims 1-24, 26-28, 33-35 and 40-47 under 35 U.S.C. 103(a) as being unpatentable over MELANA in view of THE MERCK INDEX and further in view of PAI, Applicant's amendments filed April 30, 2003 and May 16, 2003 have been fully considered and have overcome the Rejection set forth in the Office Action dated December 30, 2002.

In regards to the Rejection of claims 1-4, 7-24, 26-28, 33-35 and 40-47 under 35 U.S.C. 103(a) as being unpatentable over GILL in view of THE MERCK INDEX, Applicant's amendments filed April 30, 2003 and May 16, 2003 have been fully considered but they are not persuasive. The Rejection of the claims is maintained for the reasons of record as set forth in the Office Action dated December 30, 2002.

Response to Arguments filed April 30, 2003 and May 16, 2003

Applicant's arguments filed April 30, 2003 and May 16, 2003 have been fully considered but they are not persuasive.

In response to the argument that the specification is enabling for a wide variety of nucleosides known to inhibit reverse transcriptase, it is noted that while many nucleoside and nucleotide analogs or derivatives are known to inhibit retroviral reverse transcriptase, not all such analogs or derivatives are known to inhibit telomerase, a specialized cellular reverse transcriptase. See for example PAI et al., Cancer Research, May 1998, 58, 1909-1913; and STRAHL et al., Molecular and Cellular Biology, 1996, 16, 53-56, both previously cited. PAI teaches that 3'-azido-3'-deoxythymidine triphosphate is much more inhibitory than 2',3'-dideoxy-2',3'-didehydrothymidine triphosphate, and the cytidine analog ddCTP was not inhibitory. See abstract. STRAHL teaches that prolonged passaging in arabinofuranyl-guanosine, dideoxyinosine (ddI), dideoxyadenosine (ddA), didehydrothymidine (d4T), or phosphonoformic acid (foscarnet) did not cause reproducible telomere shortening, whereas telomerase activity was inhibited by ddGTP and AZT triphosphate. Therefore, it would not be clear to a skilled artisan at the time of filing, which nucleoside or nucleotide analogs or derivatives would be effective in the inhibition of telomerase without undue experimentation, as the art failed to establish a correlation between known inhibitors of antiviral reverse transcriptase and telomerase. The specification is not considered to have sufficient disclosure to enable the scope of the present claims and is merely considered an invitation to experiment.

In response to the argument that GILL does not teach that AZT, d4T or other reverse transcriptase inhibitors would inhibit telomerase, thereby enhancing the antitumor activity of paclitaxel, a telomere damage-inducing agent, it is noted that while GILL does not explicitly teach any synergistic benefit using the combination of AZT with paclitaxel, GILL clearly teaches that paclitaxel can be administered concurrently with AZT. See Example 6. The mere failure of

a reference to disclose all the advantages asserted by applicant is not a substitute for actual differences in properties. In re DeBlauwe, 22 USPQ 191. An apparently old composition cannot be converted into an unobvious one simply by the discovery of a characteristic one cannot glean from the cited prior art. Titanium Metals Corp. v. Banner, 227 USPQ 773. The similar compositions employed and the similar end uses envisioned indicate that the compositions of GILL would be expected to exhibit similar properties. Therefore, though GILL does not recognize the telomerase inhibitory activity of AZT, d4T or other reverse transcriptase inhibitors, this is a quantification of an inherent property of the nucleoside or nucleotide.

In response to applicant's argument that GILL fails to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., the lower dosage of the nucleoside or nucleotide inhibitor, such as AZT) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

While the unexpected results for combining a lower dosage of nucleoside or nucleotide derivative or analog, namely AZT, with a telomere damage-inducing agent, namely paclitaxel, to obtain synergistic effects for the treatment of cancer are persuasive to obviate the motivation to combine an anti-neoplastic compound of one reference with an anti-neoplastic compound of a secondary reference, the motivation for the 35 U.S.C. 103(a) rejection over GILL in view of the MERCK INDEX is based upon a different rationale. As set forth in the Office Action mailed December 30, 2002, the motivation to combine AZT and paclitaxel is clearly set forth within Example 6 of GILL. The secondary reference, the MERCK INDEX, is merely added to indicate

that other nucleoside or nucleotide analogs or derivatives are known in the art to treat AIDS, and therefore can be used concurrently with paclitaxel to treat Kaposi's sarcoma.

Similarly, VANDE WOULDE provides proper motivation to combine compounds that inhibit the G1 or S phase of the cell division cycle, such as nucleoside or nucleotide derivatives or analogs, with a compound that inhibits the M phase of the cell division cycle, such as paclitaxel, as in col. 11, lines 37-50, VANDE WOUDE discloses that the growth of oncogene-transformed cells may be completely inhibited by the combination of a drug having S-phase activity and a subtherapeutic amount of a drug having M-phase activity. The secondary reference, the MERCK INDEX, is merely added to indicate that the nucleosides zidovudine (AZT) and stavudine (d4T) are polymerase inhibitors, i.e. inhibitors of the G_1 or S phase of cell division.

In response to applicant's argument that d4T does not always effect cells in the G1 or S phase (LI et al., Anticancer Research, **1997**, *17*, 21-28) in that d4T arrests WiDr cells in the S phase, but has no effect on MCF7 cells, it is noted that such unpredictability does not preclude a skilled artisan from using d4T as an inhibitor of the G1 or S phase of the cell division cycle entirely, but simply limits the use of d4T to cell types that have been found to be susceptible to such treatment, such as in WiDr cells.

In view of the foregoing, when all of the evidence is considered, the totality of the rebuttal evidence of nonobviousness fails to outweigh the evidence of obviousness.

Inventor's Declaration under 37 CFR 1.132

The Inventor's Declaration under 37 CFR 1.132 filed on August 12, 2002 is insufficient to overcome the rejection of claims 1-24, 28, 33-35 and 40-45 under 35 U.S.C. 112, first paragraph, because the specification does not reasonably provide enablement for treating cancer using paclitaxel and any nucleoside or nucleotide analog other than AZT or d4T as set forth in the Office Action dated December 30, 2002.

In response to the argument that other reverse transcriptase inhibitors, namely suramin and pentosan polysulfate (PPS), are also telomerase inhibitors and thus synergistic with paclitaxel, it is noted that these compounds are not nucleoside or nucleotide analogs or derivatives as claimed in the present invention. Further, as set forth supra, the art at the time the invention was made fails to establish predictability with regard to the properties of the nucleosides and nucleotides analogs needed to perform the methods as instantly claimed. It is not readily apparent which nucleoside or nucleotide analog or derivative would be effective in the inhibition of telomerase without undue experimentation, as the art failed to establish a correlation between known inhibitors of antiviral reverse transcriptase and telomerase. The specification is not considered to have sufficient disclosure to enable the scope of the present claims and is merely considered an invitation to experiment.

Information Disclosure Statement

The citation of references in the responses filed April 30, 2003 and May 16, 2003, is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office.

Further, the citation of references in the responses filed April 30, 2003 and May 16, 2003, fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each U.S. and foreign patent; each publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed.

Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

Claim Objections

Claims 91 and 92 are objected to because of the following informalities: The claims use the multiple dependent claim language "any one of claims"; however the claims only recite dependency to one claim, claim 26. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Undue experimentation is a conclusion reached by weighing the noted factual considerations set forth below in In re Wands USPQ2d 14000. A conclusion of lack of enablement means that, based on the evidence regarding a fair evaluation of an appropriate combination of the factors below, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention.

These factors include

(1) quantity of experimentation necessary,

(2) the amount of guidance presented,

(3) the presence or absence of working examples,

(4) the nature of the invention,

(5) the state of the prior art,

(6) the predictability of the art and

(7) the breath of the claims.

Claims 1-24, 28, 33-35 and 40-45 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the reduction of telomere length and treatment of cancer related to human breast MCF-7 cells, pharynx FaDu cells, prostate PC3 cells and ovarian SKOV3 cells using a combination of paclitaxel and AZT or d4T, does not reasonably provide enablement for inhibiting or reducing the growth of a cell or for treating cancer using a combination of paclitaxel and a nucleoside or nucleotide analog other than AZT or d4T.

With regard to factors (1) and (2) cited above, undue experimentation is required to determine which nucleoside or nucleotide analog would be useful as a telomerase inhibitor to use for inhibiting or reducing the growth of a cell or for treating cancer for which the instant invention is applicable. There has not been provided adequate guidance in the written description for accomplishing such, as only two different nucleoside analogs were assessed, out of the numerous nucleoside and nucleotide analogs known in the art.

With regard to factors (4), (5) and (6), it is noted that there is a great deal of unpredictability in the art. For example, various nucleoside and nucleotide analogs are known as inhibitors of polymerases such as reverse transcriptase, however, not all nucleoside and nucleotide analogs are inhibitors of polymerases. Further, there is no discernable pattern as to which nucleoside and nucleotide analog will inhibit a specific polymerase, such as reverse transcriptase, and in particular telomerase. See for example PAI et al., Cancer Research, May 1998, 58, 1909-1913 (X); and STRAHL et al., Molecular and Cellular Biology, 1996, 16, 53-56 (Y). PAI teaches that 3'-azido-3'-deoxythymidine triphosphate is much more inhibitory than 2',3'-dideoxy-2',3'-didehydrothymidine triphosphate, and the cytidine analog ddCTP was not inhibitory. See abstract. STRAHL teaches that prolonged passaging in arabinofuranyl-guanosine, dideoxyinosine (ddI), dideoxyadenosine (ddA), didehydrothymidine (d4T), or phosphonoformic acid (foscarnet) did not cause reproducible telomere shortening, whereas telomerase activity was inhibited by ddGTP and AZT triphosphate. The art at the time the invention was made fails to establish predictability with regard to the properties of the nucleosides and nucleotides analogs needed to perform the methods as instantly claimed. The specification is not considered sufficient disclosure to enable the scope of the present claims and is merely considered an invitation to experiment.

With regard to factors (3) and (7), it is noted that while there are some working examples of compositions comprising AZT or d4T, it is not seen as sufficient to support the breath of the claims. It is noted that Law requires that the disclosure of an application shall inform those skilled in the art how to use applicant's alleged discovery, not how to find out how to use it for themselves. See In re Gardner et al. 166 USPQ 138 (CCPA 1970).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-4, 8-10, 12-14, 16, 18, 20, 22-24 and 40-46 are rejected under 35 U.S.C. 102(b) as being anticipated by the patent US 5,756,537 to GILL (A).

GILL teaches in Example 6 that paclitaxel can be administered concurrently with AZT for the treatment of Kaposi's sarcoma (KS). See in particular, col. 9, lines 40-42. GILL further discloses that paclitaxel can be administered orally, via inhalation, intravenously, intramuscularly, intradermally, intraperitoneally, and subcutaneously using various carriers (col. 5, line 19 to col. 6, line 4).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-4, 7-24 and 40-47 are rejected under 35 U.S.C. 103(a) as being unpatentable over GILL (A) in view of THE MERCK INDEX (W).

Applicant claims methods for the for inhibiting or reducing the growth of a cell or for treating cancer by administering paclitaxel and a nucleoside or nucleotide analog such as AZT or d4T, either serially or concurrently. Further, Applicant claims the methods wherein either each or both of the active agents are administered locally, systemically or regionally. Applicant also claims the methods wherein either each or both of the active agents are administered as a time-release formulation. Finally, Applicant claims methods wherein one of the agents can be administered in sub-therapeutic dosages.

As set forth supra, GILL teaches in Example 6 that paclitaxel can be administered concurrently with AZT for the treatment of Kaposi's sarcoma (KS). See in particular, col. 9, lines 40-42. GILL also discloses in that same section that other antiretroviral agents can be used in combination with paclitaxel. GILL further discloses that paclitaxel can be administered orally, via inhalation, intravenously, intramuscularly, intradermally, intraperitoneally, and subcutaneously using various carriers (col. 5, line 19 to col. 6, line 4).

GILL does not explicitly teach that the agents can be administered serially rather than concurrently. GILL also does not teach that d4T in particular can be administered rather than AZT.

THE MERCK INDEX teaches that stavudine (d4T) is a reverse transcriptase inhibitor for the treatment of an HIV infection. See entry no. 8958.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use another known anti-HIV agent similar to AZT, such as d4T, in combination with paclitaxel, as GILL discloses that other antiretroviral agents are viable for the treatment of Kaposi's sarcoma. A skilled artisan would have been motivated to use any known antiviral agent for the treatment of HIV concurrently or serially with paclitaxel for the treatment of HIV-related Kaposi's Sarcoma, as such regimes would be useful both in the treatment of Kaposi's Sarcoma and in the treatment of HIV. Concurrent and serial treatments are frequently used and very well known in the art pertaining to viral and cancer therapeutics. Therefore, methods regarding the various modes of administration are considered a choice of experimental design, and are well within the purview of the prior art

Claims 1-24, 26-28, 33-35, 40-47 and 90-92 are rejected under 35 U.S.C. 103(a) as being unpatentable over the patent US 6,150,398 to VANDE WOUDE et al. (B) in view of THE MERCK INDEX, **1996**, 7117, 8958 and 10252 (W).

Applicant claims methods for the for inhibiting or reducing the growth of a cell or for treating cancer by administering paclitaxel and a nucleoside or nucleotide analog such as AZT or d4T, either serially or concurrently. Further, Applicant claims the methods wherein either each or both of the active agents are administered locally, systemically or regionally. Applicant also claims the methods wherein either each or both of the active agents are administered as a time-release formulation. Applicant claims methods wherein one of the agents can be administered in

sub-therapeutic dosages. Finally, Applicant claims methods wherein the nucleoside analogs, AZT and d4T are administered at particular dosage ranges.

VANDE WOUDE teaches that paclitaxel or a paclitaxel derivative can be used with an agent that affects the G_1 or S phase of the cell division cycle. See Abstract. In col. 10, Table 3, VANDE WOUDE discloses that paclitaxel affects the M-phase, while methotrexate, 5'-fluorouracil and cytosine arabinoside effect the G_1 or S phase by altering DNA synthesis. Further, in col. 11, lines 37-50, VANDE WOUDE discloses that the growth of oncogene-transformed cells may be completely inhibited by the combination of a drug having S-phase activity and a subtherapeutic amount of a drug having M-phase activity.

VANDE WOUDE does not explicitly disclose AZT or d4T as inhibitors of the G_1 or S phase of cell division. Further, VANDE WOUDE does not specifically disclose that each or both of the active agents can be administered locally, systemically or regionally. VANDE WOUDE also does not specifically disclose that each or both of the active agents can be administered as a time-release formulation.

THE MERCK INDEX teaches that zidovudine (AZT) and stavudine (d4T) are polymerase inhibitors. See entry nos. 10252 and 8958 respectively. Further, THE MERCK INDEX discloses that AZT has antiviral, antimetabolite and antineoplastic activity.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use AZT or d4T as inhibitors of the G_1 or S phase of cell division. A skilled artisan would have been motivated to reduce or inhibit cell growth or to treat cancer with AZT or d4T and paclitaxel, as AZT and d4T are both known polymerase inhibitors, i.e. inhibitors of the G_1 or S phase of cell division. Further, the administration of the active ingredients locally,

systemically or regionally, as well as the administration of the active ingredients as a time-release formulation, is well known to one of ordinary skill in the pharmaceutical area. Therefore, methods limited to these modes of administration are considered a choice of experimental design, and are well within the purview of the prior art. Finally, it would have been obvious to one of skill in the art to administer the therapeutic agents in any effective dosage range, including subtherapeutic dosages ranges, as VANDE WOUDE teaches that the combination of drug can be administered at therapeutic or subtherapeutic levels. Therefore, the exact dosage range of the therapeutic agents of the present invention is seen as a choice of experimental design, and is considered well within the purview of the prior art.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Conclusion

Claims 1-92 are pending. Claims 25, 29-32, 36-39 and 48-89 are withdrawn. Claims 1-24, 26-28, 33-35, 40-47 and 90-92 are rejected. Claims 91 and 92 are objected to. No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Josephine Young whose telephone number is (703) 605-1201. The examiner can normally be reached on Monday through Friday, 9:00 a.m. to 6:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on (703) 308-4624. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 305-3014 for regular communications and (703) 872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

JY
July 1, 2003

JAMES O. WILSON
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600